

1 AGCATCCTGA GTAATGAGTG GCTGGGCGG GAGCAGCGGA GGTGGCCGGA GCCGTGTGGA CCAGGAGGAG CGCTTTCCAC AGGCCCTGTG GACGGGGGTG
TCGTAGGACT CATTACTCAC CGACCCCGC CTCGTCCGCT CCACCGGCT CCGCACCTT GGTCTCTC GCGAAGGTG TCCCGACAC CTGCCCCCAC
1 M S G L G R S R R G G R S R V D Q E E R F P Q G L W T G V

101 GCTATGAGAT CCGTCCCGA AGACGAGTAC TGGGATCCTC TGCTGGGTAC CTGCATGTCC TGCAAAACCA TTTCACACCA TCAGAGCCAG CGACCTGTG
CGATACTCTA GACCGGGCT TCTCGTATG ACCCTAGGAG ACGACCATG GACGTACAGG ACGTTTGGT AAACGTTGGT AGCTCGGTG AGCTCGGTG
30 A M R S C P E E Q Y W D P L L G T C M S C K T I C N H Q S Q R T C A

201 CAGCCTTCTG CAGGTCACTC AGTCCCGCA AGGACGAGG CAAGTTCTAT GACCATCTCC TGAGGGACTG CATCAGCTGT GCCTCCATCT GTGACACAGCA
GTCGGAAGAC GTCCAGTGAG TCGAGGCGT TCCTCGTTCC GTTCAAGATA CTGTAGAGG ACTCCCTGAC GTAGTCGACA CGGAGGTAGA CACCTGTCTG
64 A F C R S L S C R K E Q G K F Y D H L L R D C I S C A S I C G Q H

301 CCCTBAGCAA TGTGCATACT TCTGTAGAA CAAGCTCAGG AGCCAGTGA ACCTTCCAGG AGACGCTCAGG AGACAGCGGA GTGGAGAAGT TGAARAACAA
GGGATCTGTT ACACGTATGA AGACACTCTT GTTCGAGTCC TCGGCTCACT TGAAGGTGG TCTCGAGTCC TCTGTGCGCT CACCTCTTCA ACTTTTCTTA
97 P K Q C A Y F C E N K L R S P V N L P P E L R R Q R S G E V E N N

401 TCACACAACCT CGGGAAGGTA CCAAGGATTG GAGCACAGAG GCTCAGRAGC AAGTCCAGCT CTCGCGGGC TGAAGCTGAG TGCAGATCAG GTGGCCCTGG
AGTCTGTTGA GCCCTTCCAT GGTTCCTTAC CTCGTGTCTC CAGTCTTCG TTCAGGTGCA GAGGCCCGG ACTTCGACTC ACGTCTAGTC CACCGGAGCC
130 S D N S G R Y Q G L E H R G S E A S P A L P G L K L S A D Q V A L V

501 TCTACAGCAC GCTGGGGCTC TGCTGTGTG CCGTCTCTG CTGCTTCTG GTGGCGGTG CCGTCTCTT CAAGAAGAGG GGGATCCCT GCTCTGCCA
AGATGTCGTG CGACCCCGAG ACGGACACAC GGCAGGAGAC GACGAAGGAC CACCGCCACC GGACGAGGA GTTCTTCTCC CCGTCTAGGA CGAGGACGGT
164 Y S T L G L C L C A V L C C F L V A V A C F L K K R G D P C S C Q

601 GCCCGCTCA AGGCCCGCTC AAGTCCGGC CAAGTCTTCC CAGGATCAG CGATGGAAGC CGGAGCCCT GTGACACAT CCCCCGAGCC AGTGGAGACC
CGGGGCGAGT TCCGGGCGG TTTCAGGCG GTTCAAGAGG GTCTAGTGC GCTACCTTCG GCGGTGCGGA CACTCGTGTG GGGGCTCGG TCACCTCTGG
197 P R S R P R Q S P A K S S Q D H A M E A G S P V S T S P E P V E T

701 TGCAGTTCT GCTTCCCTGA GTGCAGGGG CCCAGCGAGG AGAGCGCAGT CACGCTGGG ACCCCGACC CCACCTTGTG TGAAGGTGG GGTGCCACCA
ACGTCGAAGA CGAAGGACT CACGTCCCGC GGGTCCGTCC TCTCGGTCA GTGCGGACCC TGGGGGCTGG GGTGAACAGG ACCTTCCACC CCGCGGTGT
230 C S F C F P E C R A P T Q E S A V T P G T P D P T C A G R W G C H T

801 CCAGGACCAC AGTCTGCGAG CCTTGCCAC ACATCCCGA CAGTGGCCTT GGCATTGTGT GTGTGCCTGC CCAGGAGGGG GCGCCAGGTG CATAAATGGG
GGTCTGGTG TCAGGACGTC GGAAGGGGTG TGTAGGTCT GTACCCGNA CCGTAACACA CACACGAGG GGTCTCCCG CCGGTCCAC GTATTTACCC
264 R T T V L Q P C P H I P D S G L G I V C V P A Q E G G P G A O

GenBank

901 GGTGAGGGAG GGAAGGAGG AGGAGAGAG ATGAGAGAG GGGAGAGGG AAAGAGAGT GGGAGAGGG GAGAGAGATA TGAGGAGAGA GAGACAGAGG
 CCAGTCCCTC CTTTCCCTCC TCCCTCTCTC TACCTCTCTC CCCCCTCTCC TTCTCTCTCA CCCCCTCTCC CTCTCTCTAT ACTCCTCTCT CTCTGTCTCC

1001 AGGCAGAAAG GGACAGAAAC AGAGAGACA GAGAGGAGA GAGAGAGAGA GAGAGAGGG AACAGAGGCA GAGAGGAAA GAGGCAGAGA
 TCCGTCTTTC CCTCTCTTTG TCTCTCTGT CTCTCCCTCT CTCTCTGTCT CCCCCTCTCT CTGTCTCCCC TTCTCTCCGT CTCTCCCTTT CTCCGTCTCT

1101 AGGAAGAGA CAGGCAGAGA AGGAGAGAG CAGAGAGGGA GAGAGAGAGA GAGAGAGAGA GGCAGAGAGA CAGAGAGGGA GAGAGGACA GAGAGAGATA
 TCCCTTCTCT GTCCGTCTCT TCCCTCTCTC GTCTCTCCCT CTCTCCGTCT CTCCCTCTCT CCGTCTCTCT GTCTCTCCCT CTCTCCCTGT CTCTCTCTAT

1201 GAGCAGGAGG TCGGGGCACT CTGAGTCCCA GTTCCAGTG CAGCTGTAGG TCGTCATCAC CTACCCACAC GTGCATATAA GTCCTCGTGC CTGCTGCTCA
 CTGCTCCTCC AGCCCCGTGA GACTCAGGT CAAGGTCTAC GTCACATCC AGCAGTAGTG GATTGCTGTG CACGTATTTT CAGGAGCAGG GACGACGAGT

1301 CAGCCCCCGA GAGCCCCCTCC TCCTGGAGAA TAAACCTTT GGCAGCTGCC CTTCCTCAA AAAAAAAA AAAAAA
 GTCGGGGGCT CTCGGGGAGG AGGACCTCTT ATTTTGAAG CCGTCGACGG GAAGGAGTTT TTTTTTTTTT TTTTTT

Fig. 1B

Fig. 2

1 AAGACTCAAA CTTAGAACT TGAATTAGAT GTGTATTCA AATCCTTACG TGCCGCGAAG ACACAGACAG CCCCCTAAG AACCCACGAA GCAGGCGAAG
TTCTGAGTTT GAATCTTTGA ACTTAATCTA CACATAAAGT TTAGGAATGC ACGGGCTTC TGTGTCTGTC GGGGGCATTC TTGGGTGCTT CGTCCGCTTC

101 TTCAATTGTT TCAACAATTCT AGCTGCTCTT GCTGCATTGG CTCTGGAATT CTGTAGAGA TATTACTTGT CCTTCCAGGC TGTCTTTCT GTAGCTCCCT
AAGTAACAAG AGTTGTAAGA TCGACGAGAA CGACGTAAAC GAGACCTTAA GAACATCTCT ATAATGAACA GGAAGTCCG ACAAGAAAGA CATCGAGGGA

201 TGTCTTCTTT TTGTGATCAT GTTGCAGATG GTGGGCGAGT GCTCCAAAA TGAATATTTT GACAGTTTGT TGCATGCTTG CATACCTTGT CAACCTTCGAT
ACAAAAGAAA AACACTAGTA CAACGCTCTAC CGACCCGTCA CGAGGGTTTT ACTTATAAAA CTGTCAAACA ACGTACGAAC GTATGGAACA GTTGAAGCTA
1 Me tLeuGlnMet AlaGlyGlnC ysSerGlnAs nGluTyrPhe AspSerLeuL euHisAlaCy sileProCys GlnLeuArgC

301 GTTCTTCTAA TACTCTCTCT CTAACATGTC ACGTTTATTG TAATGCAAGT GTGACCAATT CAGTGAAGG AACGAATGCG ATTCTCTGGA CCTGTTTGGG
CAAGAGATT ATGAGGAGGA GATTGTACAG TCGCAATAAC ATTACGTTCA CACTGGTTAA GTCACCTTCC TTGCTTACGC TAAGAGACCT GGACAAACCC
29 ysSerSerAs nThrProPro LeuThrCysG lnaArgTyrCy sAsnAlaSer ValThrAsnS erValLysG l yThrAsnAla IleLeuTpt hrCysLeuG l

401 ACTGAGCTTA ATAATTTCTT TGGCAGTTTT CGTGCTAATG TTTTTCGTAA GGAAGATAAG CTCTGAACCA TTAAGGAGCG AGTTTAAAAA CACAGGATCA
TGACTCGAAT TATTAAAGAA ACCGTCAAAA GCACGATTAC AAAAAGCATT CCTTCTATTG GAGACTTGGT AATTCTCTGC TCAAAATTTT GTGTCTCTAGT
62 yLeuSerLeu IleIleSerL euAlaValPh eValLeuMet PheLeuLeuA rgLysIleSe rSerGluPro LeuLysAspG luPheLysAs nThrGlySer

501 GGTCTCCTGG GCATGGCTAA CATTGACCTG GAAAGAGCA GGACTGGTGA TGAATATTAT CTTCCGAGAG GCCTCGAGTA CACGGTGGAA GAATGCACCT
CCAGAGGACC CGTACCGATT GTAACCTGAC CTTTCTCGT CCTGACCACT ACTTTAATAA GAAGGCTCTC CGAGACTCAT GTGCCACCTT CTTACGTGGA
95 GlyLeuLeuG lyMetAlaAs nIleAspLeu GluLysSerA rgThrGlyAs pGluIleIle LeuProArgG lyLeuGluTy rThrValGlu GluCysThrC

601 GTGAAGACTG CATCAAGAGC AAACCGAAGG TCGACTCTGA CCATTGCTTT CCACTCCAG CTATGGAGGA AGCGCAACC ATTCTTGTC A CCACGAAAC
CACTTCTGAC GTAGTTCTCG TTTGGCTTCC AGCTGAGACT GGTAAACGAAA GGTGAGGTC GATACCTCCT TCCGCGTTGG TAAGAACAGT GGTGCTTTTG
129 ysGluAspCy sileLysSer LysProLysV alAspSerAs pHisCysPhe ProLeuProA laMetGluG l uGlyAlaThr IleLeuValT hrThrLysTh

701 GAATGACTAT TGCAGAGGCC TGCCAGCTGC TTTGAGTGTG ACGGAGATAG AGAATCAAT TTCTGCTAGG TAATTAACCA TTTCGACTCG AGCAGTGCCA
CTTACTGATA ACGTTCTCGG ACGGTCGACG AAACCTCACG TGCCTCTATC TCTTTAGTTA AAGACGATCC ATTAATTGGT AAAGCTGAGC TCGTCACGCT
162 rAsnAspTyr CysLysSerL euProAlaAl aLeuSerAla ThrGluIleG lylLysSerIl eSerAlaArg OC*

801 CTTTAAAAAT CTTTGTTCAG AATAGATGAT GTGTCAGATC TCTTTAGGAT GACTGTATTT TTCAGTTGCC GATACAGCTT TTTGTCTCTT AACTGTGGAA
GAAATTTTGA GAAACAGTC TTATCTACTA CACAGTCTAG AGAAATCCTA CTGACATAAA AAGTCAACCG CTATGTCGAA AACACAGGAG TTGACACCTT

901 ACTCTTTTATG TTAGATATAT TTCTCTAGGT TACTGTTGGG AGCTTAATGG TAGAACTTC CTTGGTTTCA TGATTAAAGT CTTTTTTTTT CCTGA
TGAGAAATAC AATCTATATA AAGAGATCCA ATGACAACCC TCGAATTACC ATCTTTGAAG GAACCAAACT ACTAATTTCA GAAAAAANA GGAAT

Object "The43460" Fig. 4A

1 GGTACGAGGC TTCTAGAGG GACTGGAACC TAATTCTCCT GAGGCTGAGG GAGGTGGAG GGTCTCAAGG CAACGCTGGC CCCACGACGG AGTGCCAGGA
 CCATGCTCCG AAGGATCTCC CTGACCTTGG ATTAAGAGGA CTCGACTCC CTCCACCTC CCAGAGTTCC GTTGGACCG GGTGCTGCC TCACGGTCTCT

 101 GCACTAACAG TACCTTAGC TTGCTTTTCT CTCCCTCCT TTTATTCTC AAGTTCCTTT TTATTCTCC TTGGTAACA ACCTTCTTCC CTTCTGCACC
 CGTGATTGTC ATGGGAATCG AACGAAAGGA GGAGGGAGGA AAATAAAG TTAAGGAAA AATAAGAGG AACGATTGT TGAAGAAGG GAAGACGTGG

 201 ACTGCCCGTA CCTTACCGG CCCGGCCACC TCCTTGCTAC CCACCTCTG AACACACAGC TGTTGGCAGG GTCCCCAGCT CATGCCAGCC TCAICTCTCT
 TGACGGGCAT GGAATGGGC GGGGCGGTGG AGGAACGATG GGTGAGAAC TTTGTTGTCG AACACCGTCC CAGGGTCTGA M P A S S P F
 1

 301 TCTTGCTAGC CCCAAAGG CCTCCAGGCA ACATGGGGG CCAGTCAGA GAGCGGCAC TCTCAGTTG CCTCTGGTTG AGTTGGGGG CAGCTCTGGG
 AGAACGATCG GGGGTTTCCC GGAGGTCCGT TGTACCCCCC GGTCCAGTCT CTCGGCCGTG AGAGTCAACG GGAGACCAAC TCAACCCCCC GTCGAGACCC
 8 L L A P K G P P G N M G G P V R E P A L S V A L W L S W G A A L G

 401 GCGCGTGGCT TGTGCCATGG CTCTGCTGAC CCAACAACA GAGTGCAGA GCCTCAGGAG AGAGTGAGC CGGCTGCAGG GGACAGGAG CCCCTCCCAG
 CCGGCACCGA ACACGGTACC GAGACGACTG GGTGTTTGT CTGACGCT CTGAGTCTCTC TCTCCACTCG GCCGACGTCC CTTGTCTTCC GGGAGGGTCT
 41 A V A C A M A L L T Q Q T E L Q S L R R E V S R L Q G T G G P S Q

 501 AATGGGGAAG GGTATCCCTG GCAGAGTCTC CCGAGACAGA GTTCCGATG CCTTGAAGC TGGGAGAATG GGGAGAGATC CCGGAAAAGG AGACAGTGC
 TTACCCCTTC CCATAGGAC CGTCTCAGAG GGCCTCGTCT CAAGGCTAGG GACCTTCG ACCCTCTTAC CCCTCTCTAG GGCCTTTTCC TCTGCTCACG
 74 N G E G Y P W Q S L P E Q S S D A L E A W E N G E R S R K R R A V L

 601 TCACCCCAAA ACAGAAGAAG CAGCACTCTG TCCTGCACT GGTCCCACT AACGCCACT CCAGGATGA CTCGATGTG ACAGAGTGA TGTGGCAACC
 ACTGGGTTT TGTCTTCTC GTCGTGAGAC AGACGCTGGA CCAAGGGTAA TTGCGGTGGA GGTCTCTACT GAGCTACAC TGTCTCCACT ACACCGTTGG
 108 T Q K Q K K Q H S V L H L V P I N A T S K D D S D V T E V M W Q P

 701 AGCTCTTAGG CGTGGGAGG GCCTACAGC CCAAGGATAT GGTGTCCGAA TCCAGGATGC TGGAGTTTAT CTGCTGTATA GCCAGTCTCT GTTCAAGAC
 TCGAGAATCC GCACCCCTC CGATGTCCG GGTCTCTATA CCACAGGCTT AGTCTCTAGC ACCTCAAATA GACGACATAT CGGTCCAGGA CAAAGTTCTG
 141 A L R R G R G L Q A Q G Y G V R I Q D A G V Y L L Y S Q V L F Q D

 801 CTGACTTTCA CCATGGGTCA GGTGGTGTCT CGAGAAGGCC AAGGAAGGCA GGAGACTCTA TTCGGATGA TAAGAAGTAT GCCCTCCCAC CCGGACCGGG
 CACTGAAGT GGTACCAGT CCACCACAGA GCTCTTCCG GTCTTCCG TCTCTGAGT AAGCTACAT ATTCTTATA CCGGAGGGTG GGCCTGGCCC
 174 V T F T M G Q V V S R E G Q G R Q E T L F R C I R S M P S H P D R A

 901 CCTACACAG CTGCTATAGC GCAGGTGTCT TCATTTTACA CCAAGGGGAT ATTCTGAGTG TCATAATTCC CCGGGCAAGG CGAAACTTA ACCTCTCTCC
 GGATGTTGTC GACGATATCG CGTCCACAGA AGGTAAATGT GGTCCCTCTA TAAGACTCAC AGTATTAGG GGCCTGTCC CGCTTTGAAT TGGAGAGAGG
 208 Y N S C Y S A G V F H L H Q G D I L S V I I P R A R A K L N L S P

1001 ACATGGRACC TTCCTGGGGT TTGTGAARACT GTGTTGTGTTGTTTATATAAAATGGGTCGCGAGGTCGACCTTCTGGTCCACCCCATGTATGACCTCTGTCGGTTCT
TGTACCTTGGAGGACCCCAACACATTGACACTAACACAATATTTTCA
241 H G T F L G F V K L O
1101 GCTGAGTATA TAAAGGAGAG GGAATGTGCA GGAACAGAGG CATCTTCCTG GTTTGGCTC CCGTTCCTC ACTTTCCCT TTTCAATCCC ACCCCCTAGA
CGACTCATAT ATTCCTCTC CCTTACCGT CCTGTCTCC GTAGAAGGAC CCAACCGAG GGCACAGGAG TGAAGAAGGA AAAGTAAGGG TGGGGATCT
1201 CTTTGATTT ACGGATACT TGCTTCTGTT CCCCATGGAG CTCGAATTC TTGCGTGTGT GTAGATGAGG GCGGGGGAC GGGCGCCAGG CATGTTCAG
GAAACTAATA TGCCTATAGA ACGAAGACAA GGGGTACCTC GAGGCTTAAG AACGCACACA CATCTACTCC CCGCCCCCTG CCGCGGTCC GTACAAGTC
1301 ACCTGTGCG GGGCCACTGG AAGCATCCAG AACAGCACCA CCATCTTA
TGGACCAGCC CCGGGTGACC TTCGTAGGTC TTGTCGTGTT GTAGAAT

Fig. 4B

FIGURE 5A

PRO	XXXXXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXXYYYYYYYY	(Length = 12 amino acids)

% amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

5 divided by 15 = 33.3%

FIGURE 5B

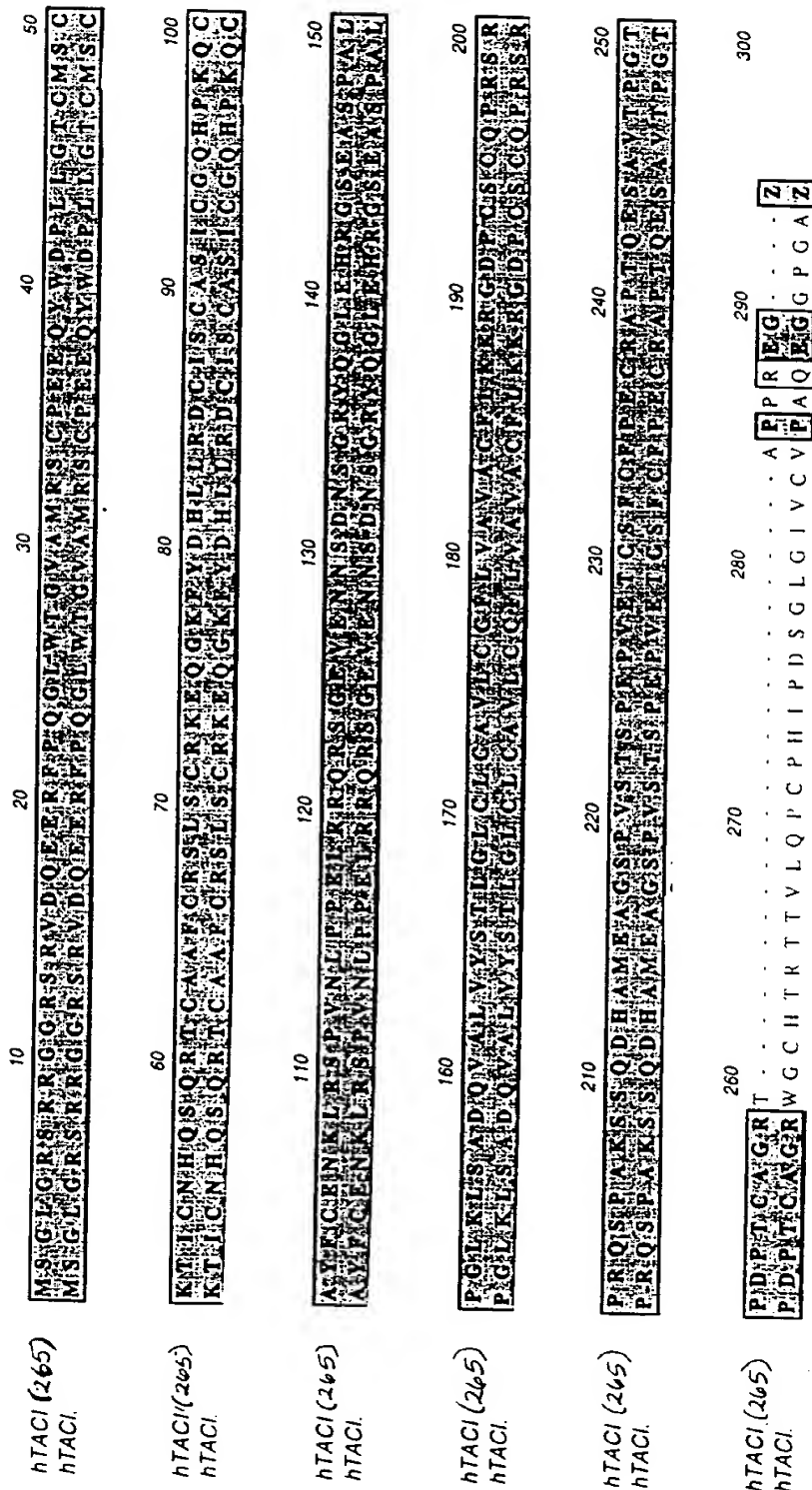
PRO	XXXXXXXXXXXX	(Length = 10 amino acids)
Comparison Protein	XXXXXXYYYYYYZZYZ	(Length = 15 amino acids)

% amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

5 divided by 10 = 50%

Fig. 6



[illegible]

Fig. 7

(A)

Flag-Light				Flag-April				Flag-Blys/TAIL-1
DcR3	Tac	BCMA	prK	DcR3	Tac	BCMA	prK	DcR3

218 —
108 —
67 —
44 —
28 —
19 —
14 —

(B)

Flag-Blys/TAIL-1			Flag AP-April	Flag AP-Blys/TAIL-1	
Tac	BCMA	prK	DcR3	Tac	BCMA

218 —
108 —
67 —
44 —
28 —
19 —
14 —

Flag-AP-Blys/TAIL-1			prK		
BCMA	prK	DcR3	Tac	BCMA	prK

218 —
108 —
67 —
44 —
28 —
19 —
14 —

Ip: with protein A
WB with α Flag HR

Fig. 8

(D)

Flag-Light c				Flag-Apr.1				Flag-BLys/TAH-1				Flag Ap Apr.1				Flag AP BLys/TAH-1	
DeR3	Tac	BcMA	PrK	DeR3	Tac	BcMA	PrK	DeR3	Tac	BcMA	PrK	DeR3	Tac	BcMA	PrK	DeR3	Tac
1A	1B	1C	1D	2A	2B	2C	2D	3A	3B	3C	3D	4A	4B	4C	4D	5A	5B

218
169
127
94
28
19
14

—
—
—
—
—
—
—
—

Flag Ap BLys/TAH-1		PrK	
BcMA	PrK	DeR3	Tac
BcMA	PrK	BcMA	PrK
5C	5D	6A	6B
6C	6D		

—
—
—
—
—
—
—
—

Ip: with

α Flag

WB: with

α Hu IgG-HRP

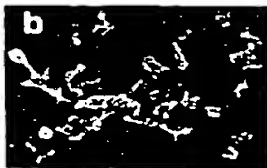
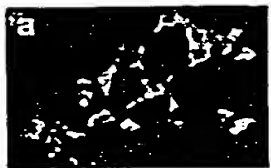
Fig. 8

Fig. 8H

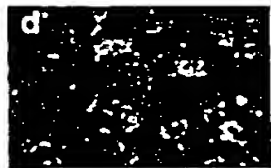
008277 The 260

9A

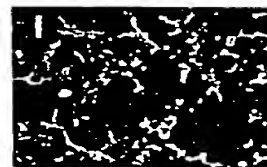
Blys/
TALL-1



April



TNFa



BCMA-hFC

TACI-hFC

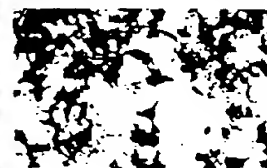
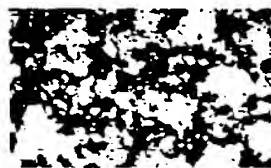
TNFR1-hFC

9B

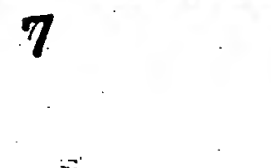
TACI



BCMA



Vector



AP-Blys/TALL-1

AP-April

AP-TNFα

Fig. 9

008211-14260
IgM μ g/ml

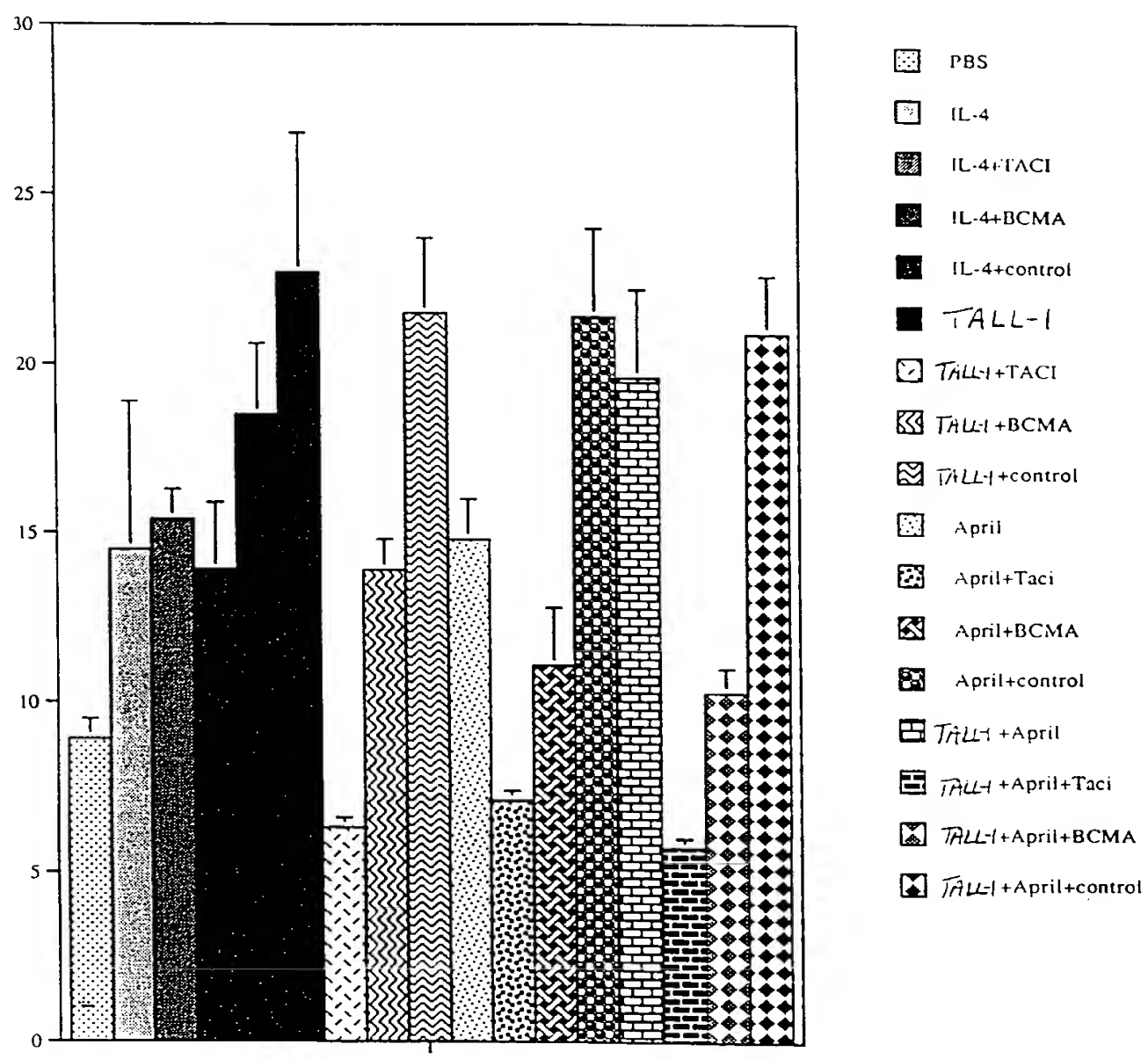


Fig. 10

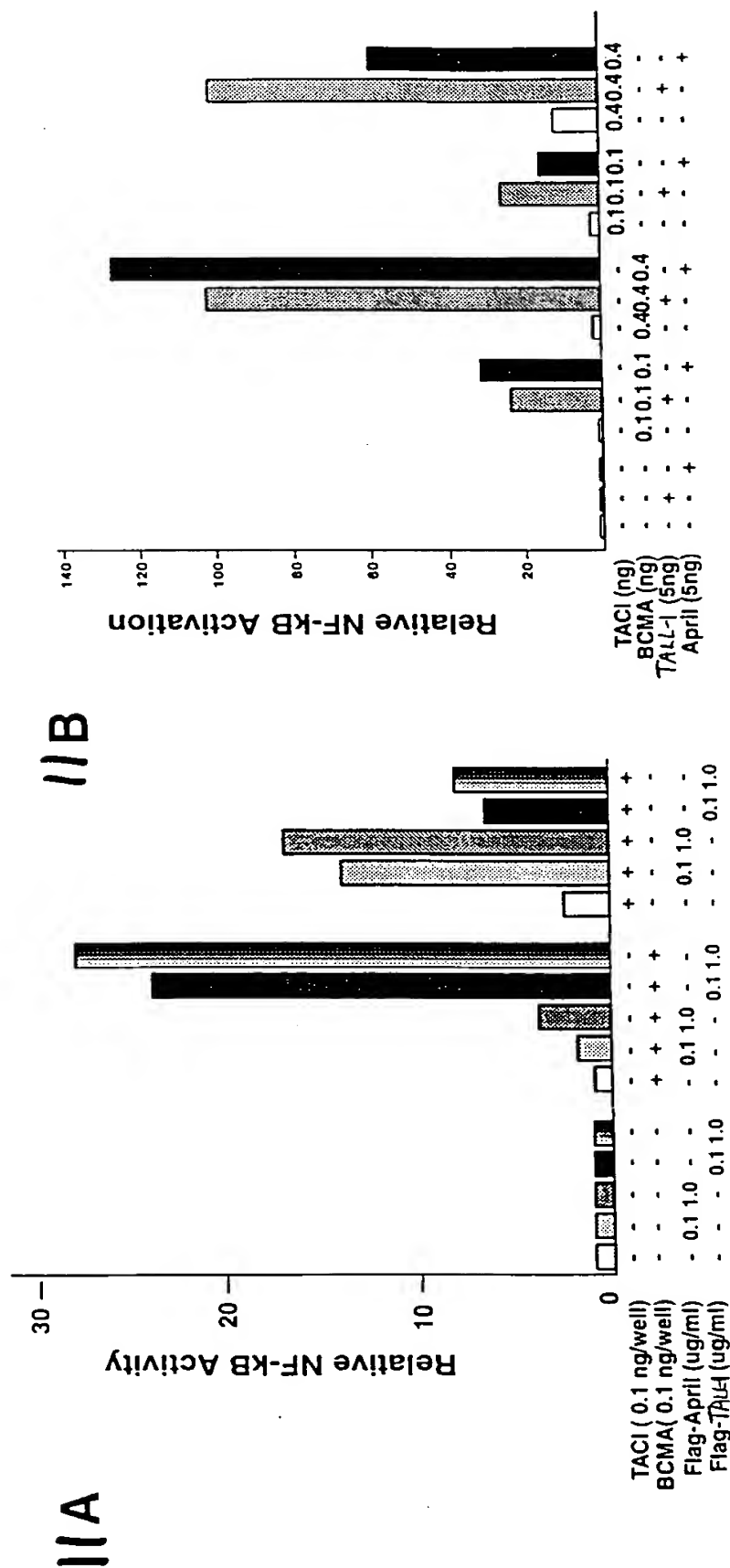


Fig. 11c

008277 14E42650

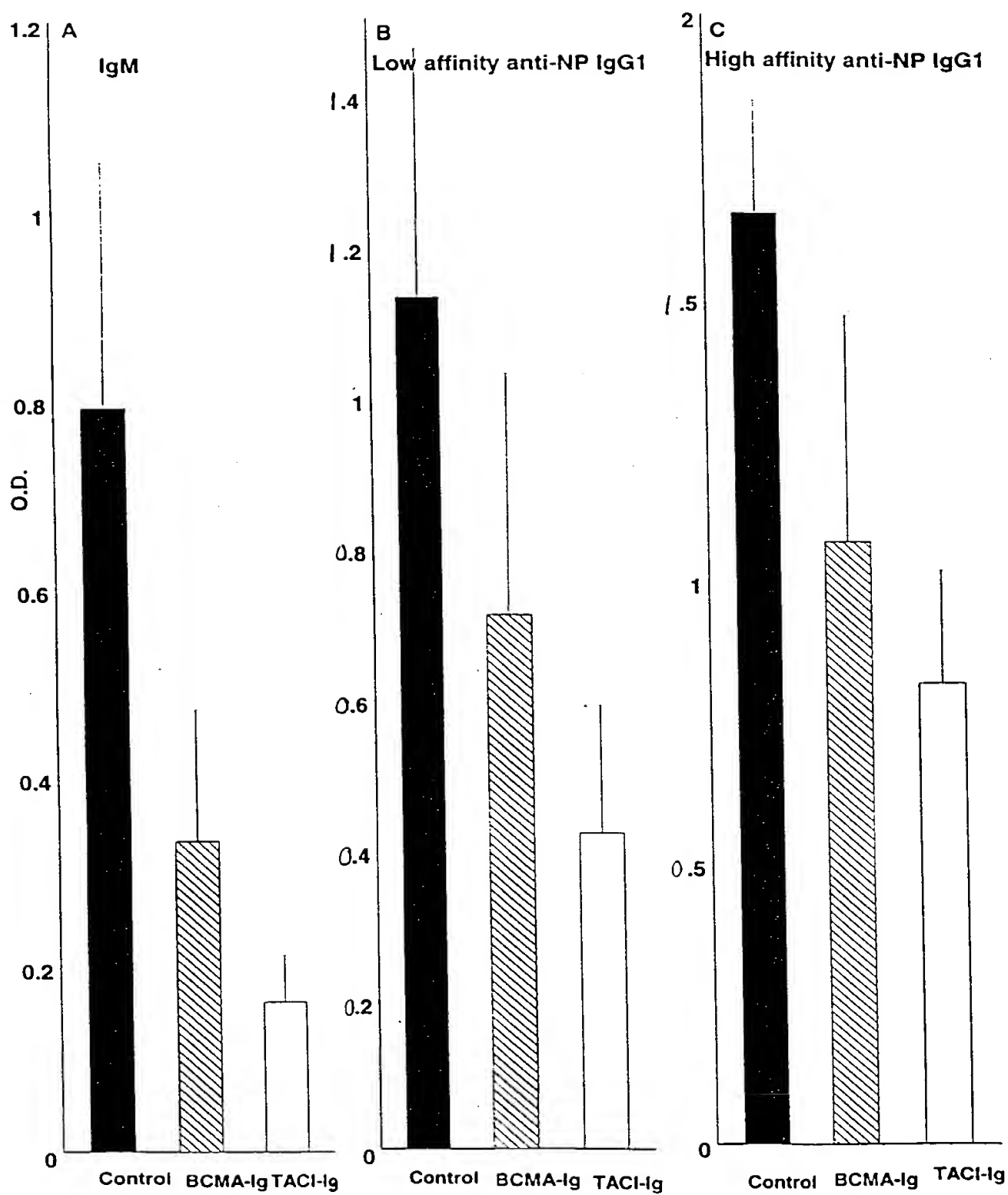


Fig. 12

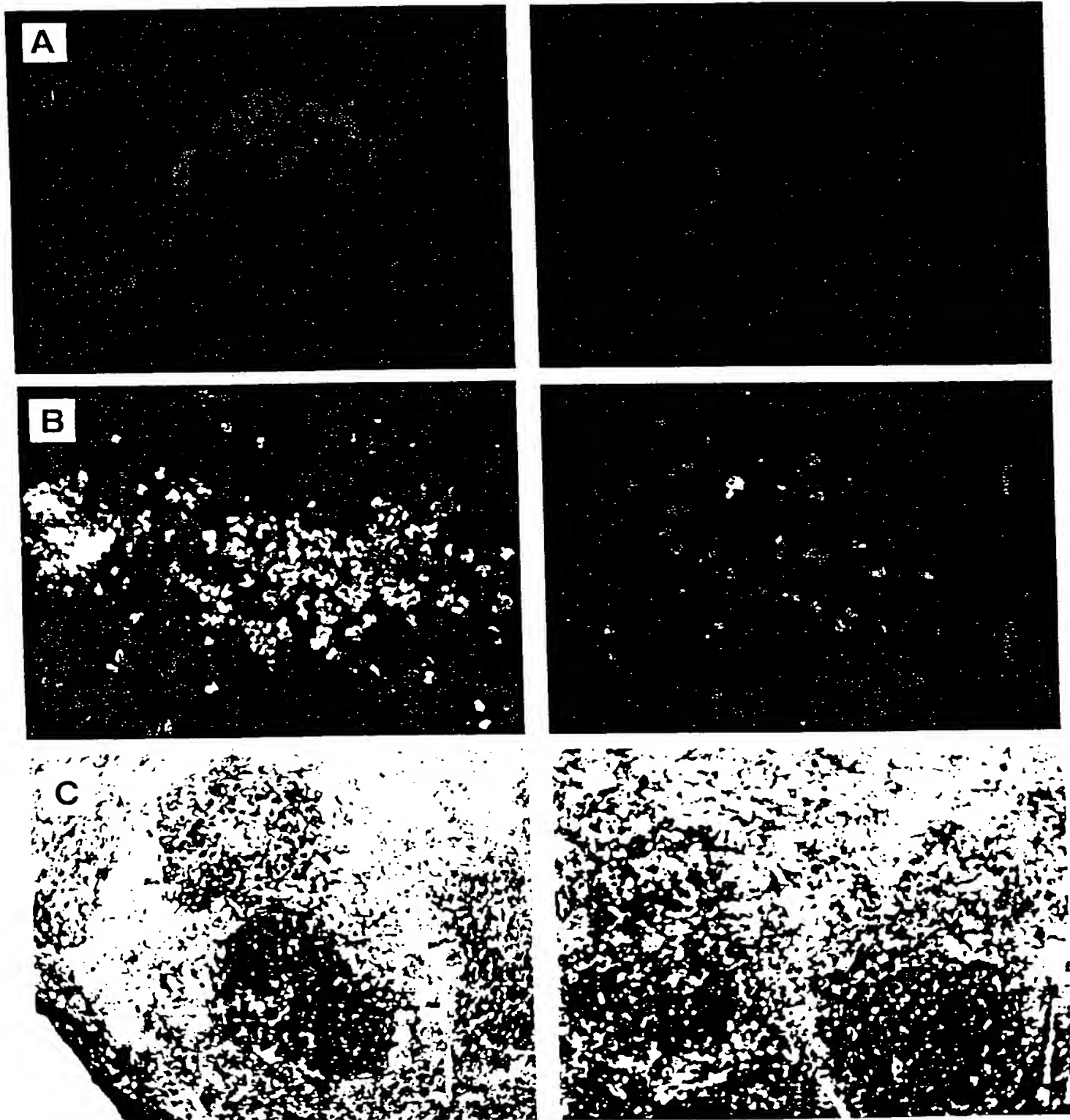


Fig. 13-1

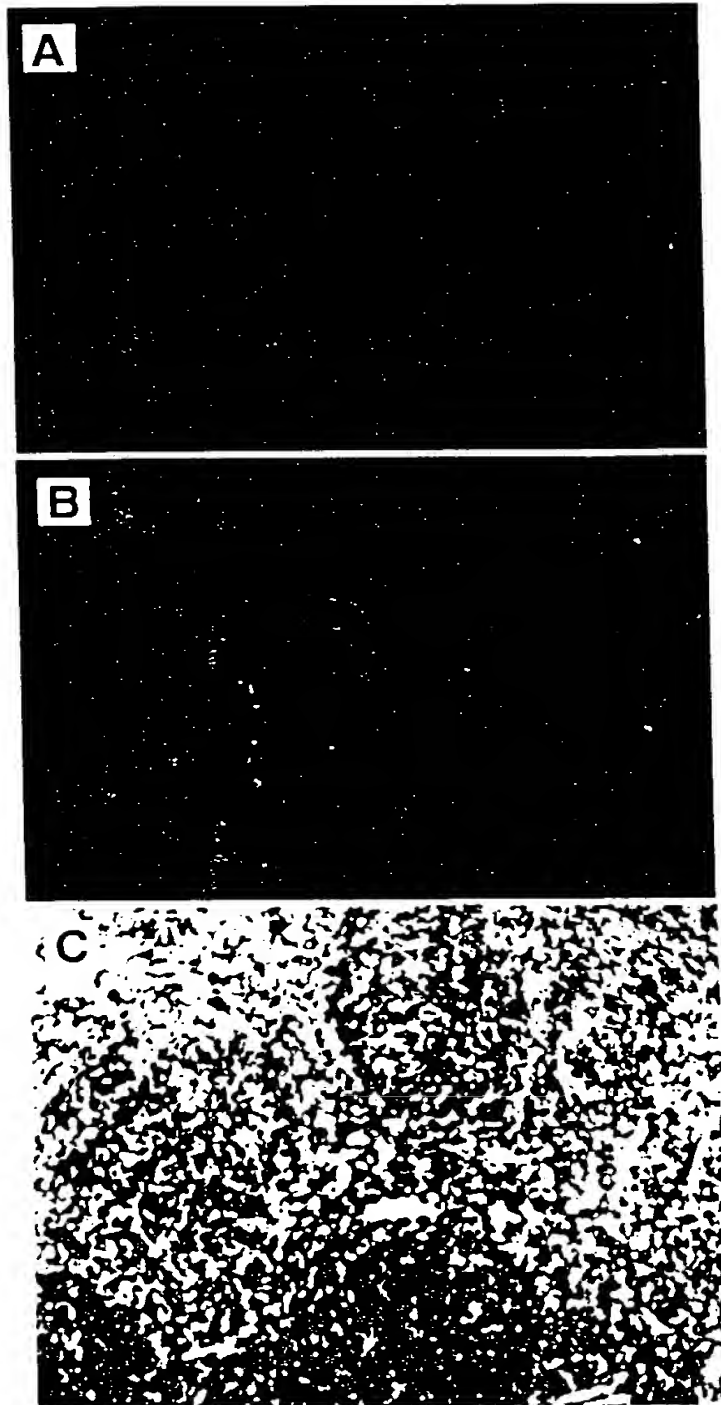


Fig. 13-2

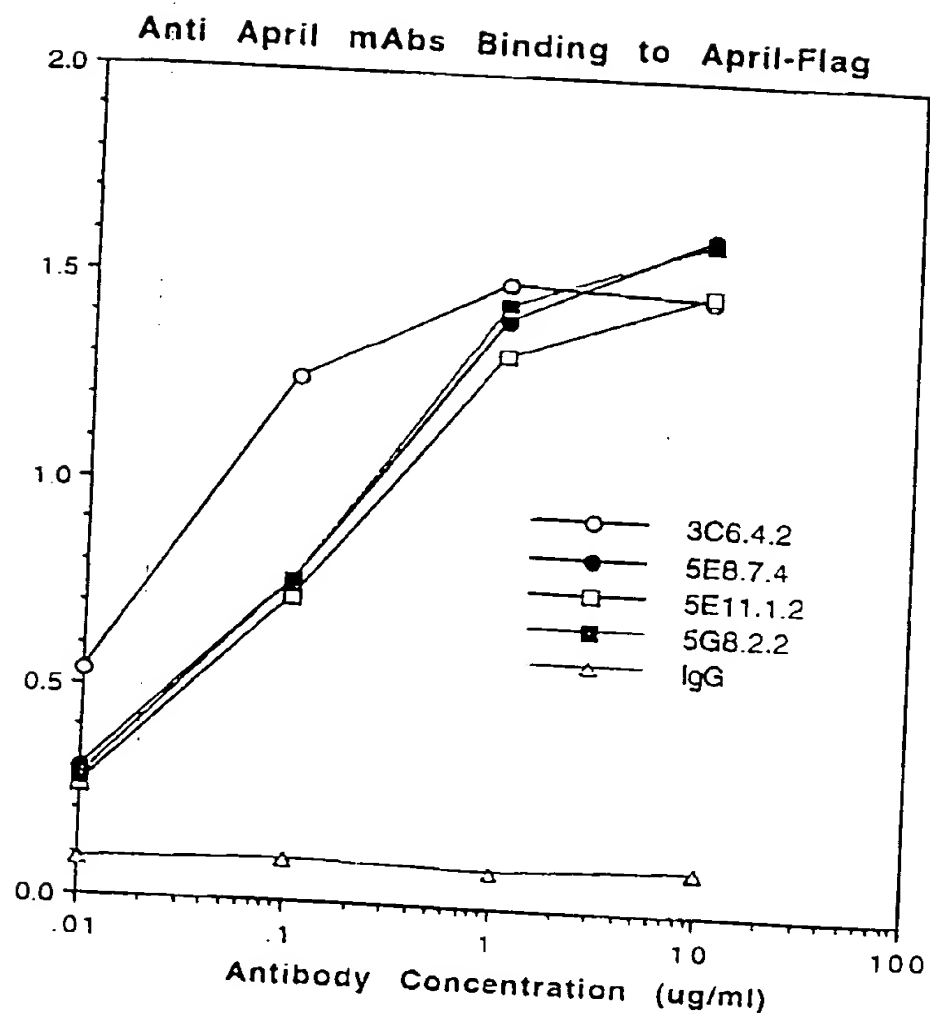


Fig. 14A

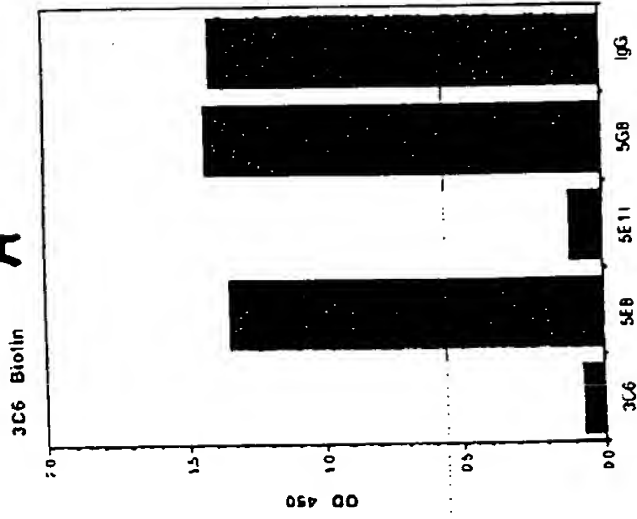
Summary of antiApril mABs

mAb	Isotype	Epitope	Binding (ELISA)		Block April binding to	
			April	TALI	BCMA	TACI
3C6.4.2	IgG2a	C	++	-	+++	+
5E8.7.4	IgG2a	A	++	-	-	-
5E11.1.2	IgG1	C?	++	-	+	+
5G8.2.2	IgG2a	B	++	-	-	-

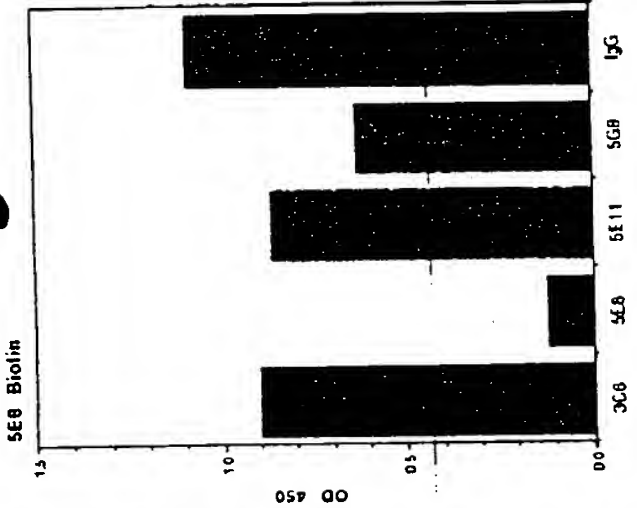
MAB 5E11.1.2 may bind to the similar epitope.

Fig. 14B

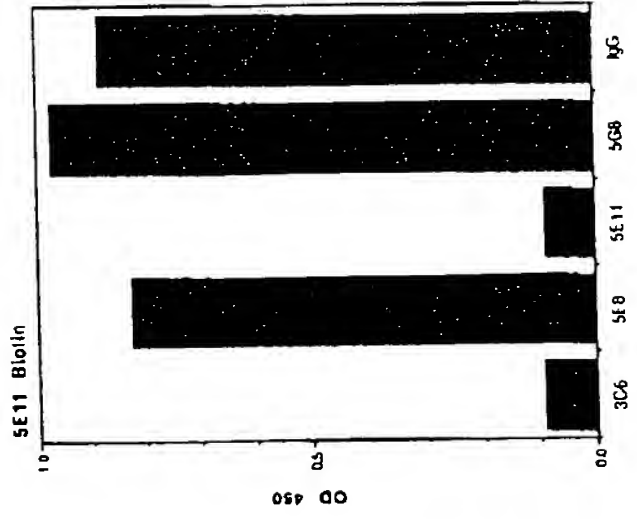
A



B



C



D

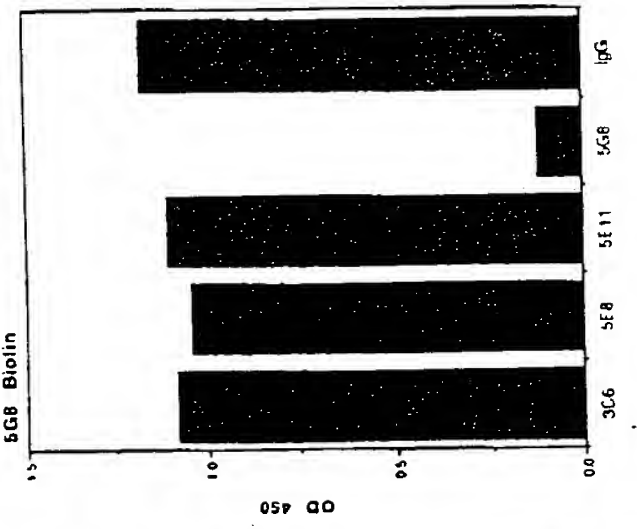


Fig. 15

B

INDIVIDUAL PAW ARTHRITIC SCORE

TACI-Fc Saline Control IgG

Fig. 16B

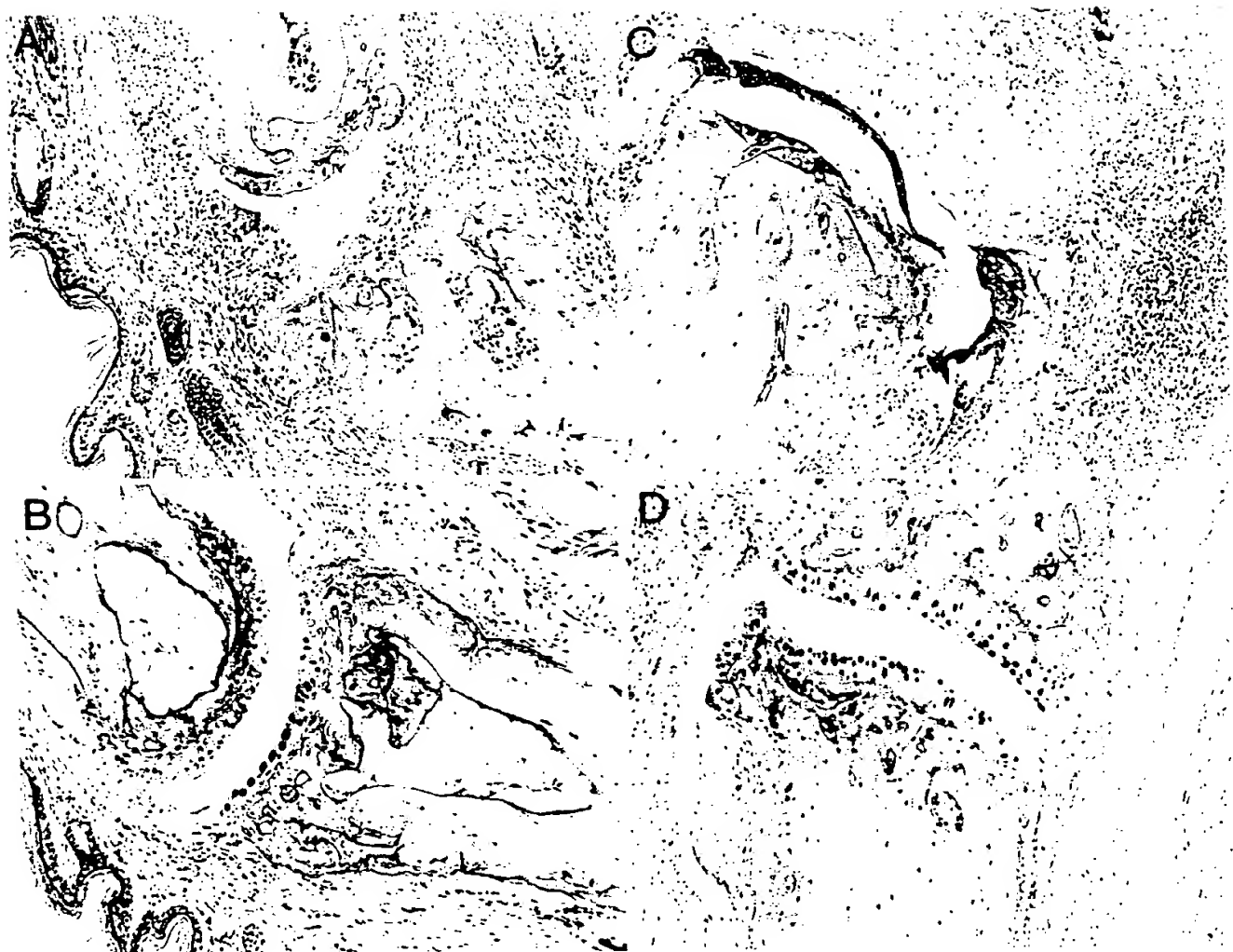


Fig. 17A-D

09724341. 112800

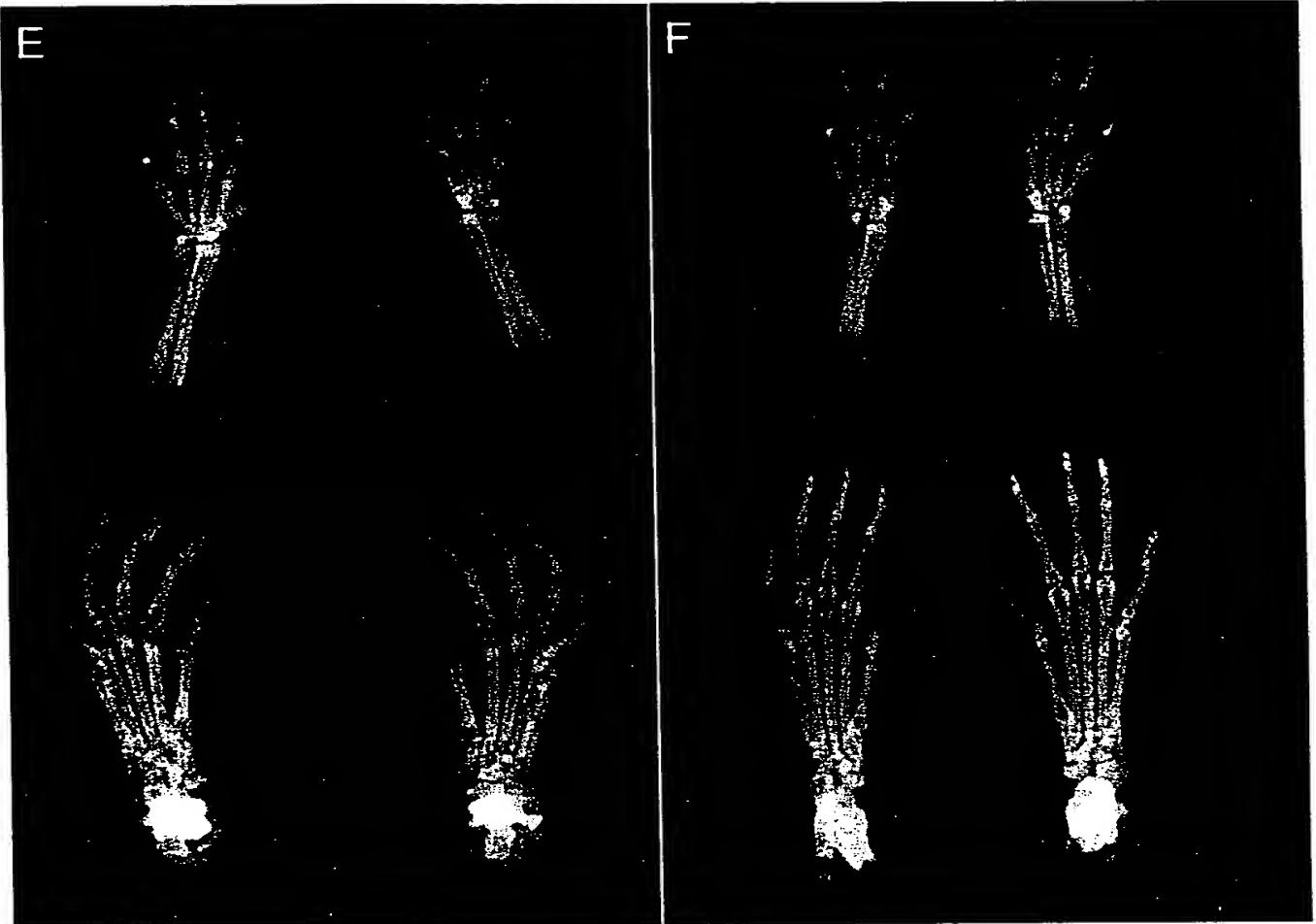


Fig. 17E-F

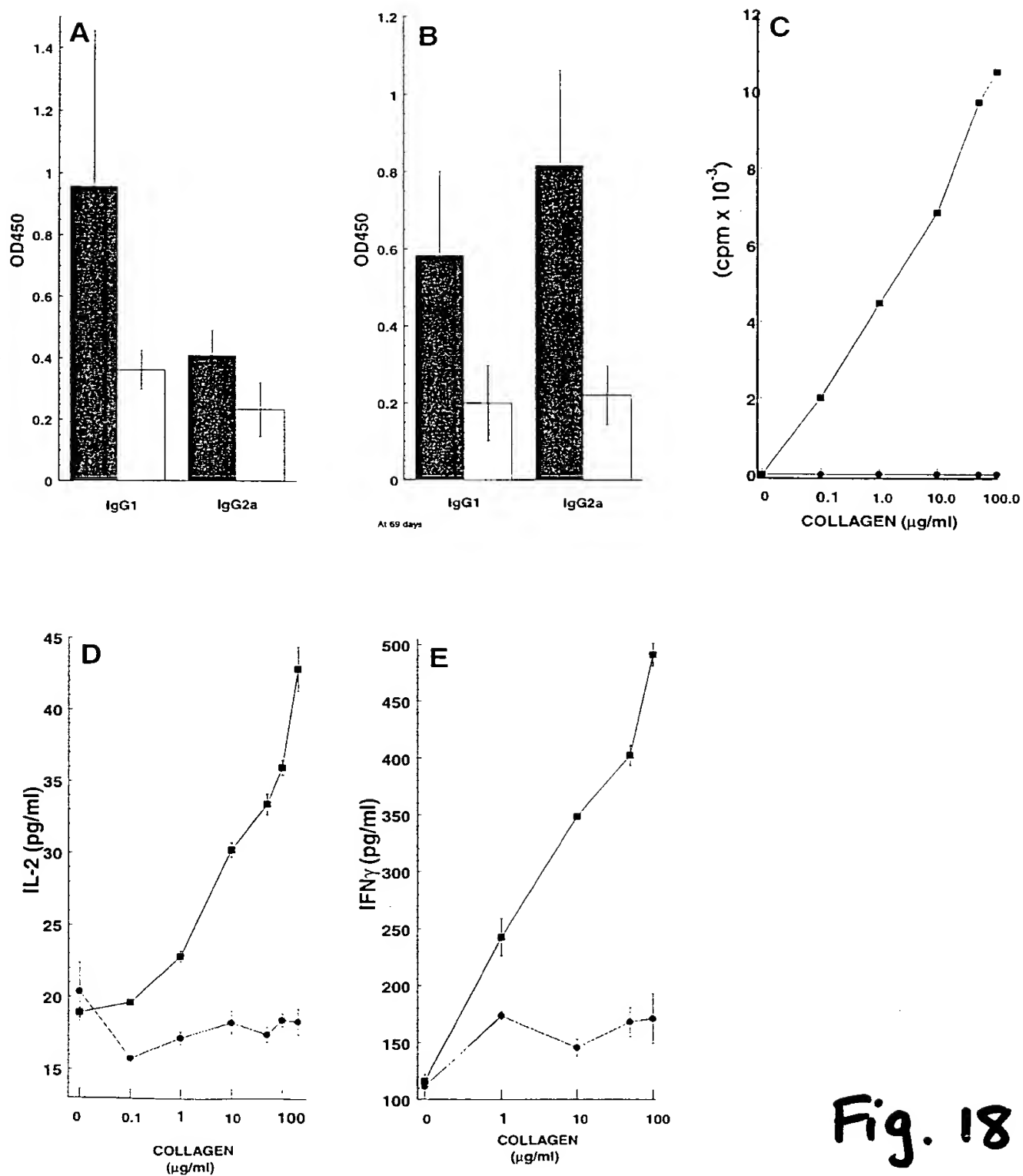


Fig. 18

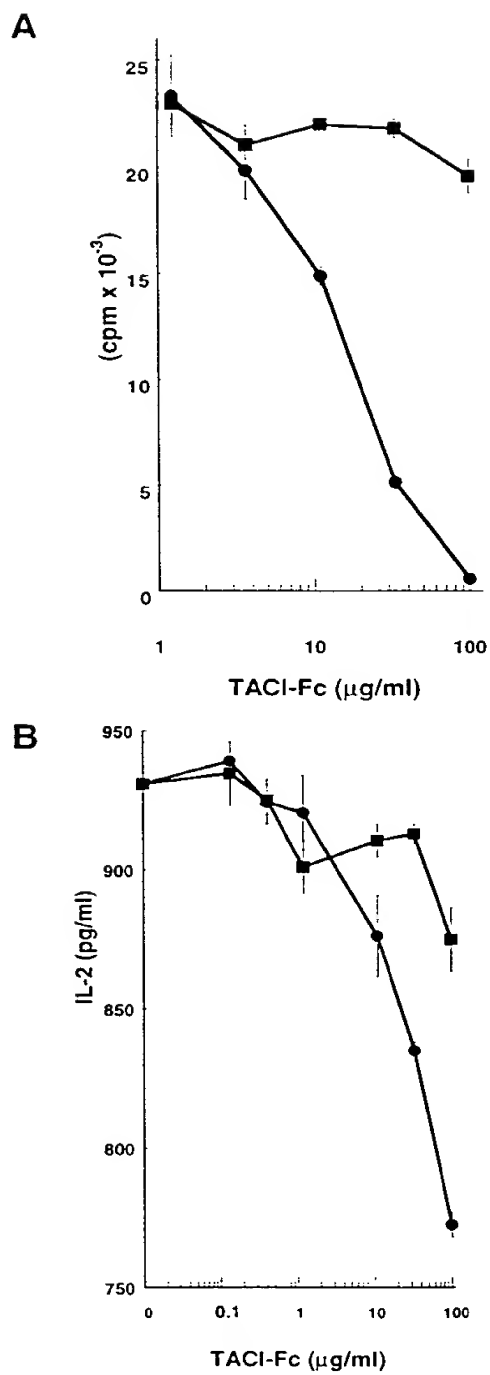


Fig. 19

TACI-Fc treatment of mice inhibits EAE in MBP-TCR transgenic mice

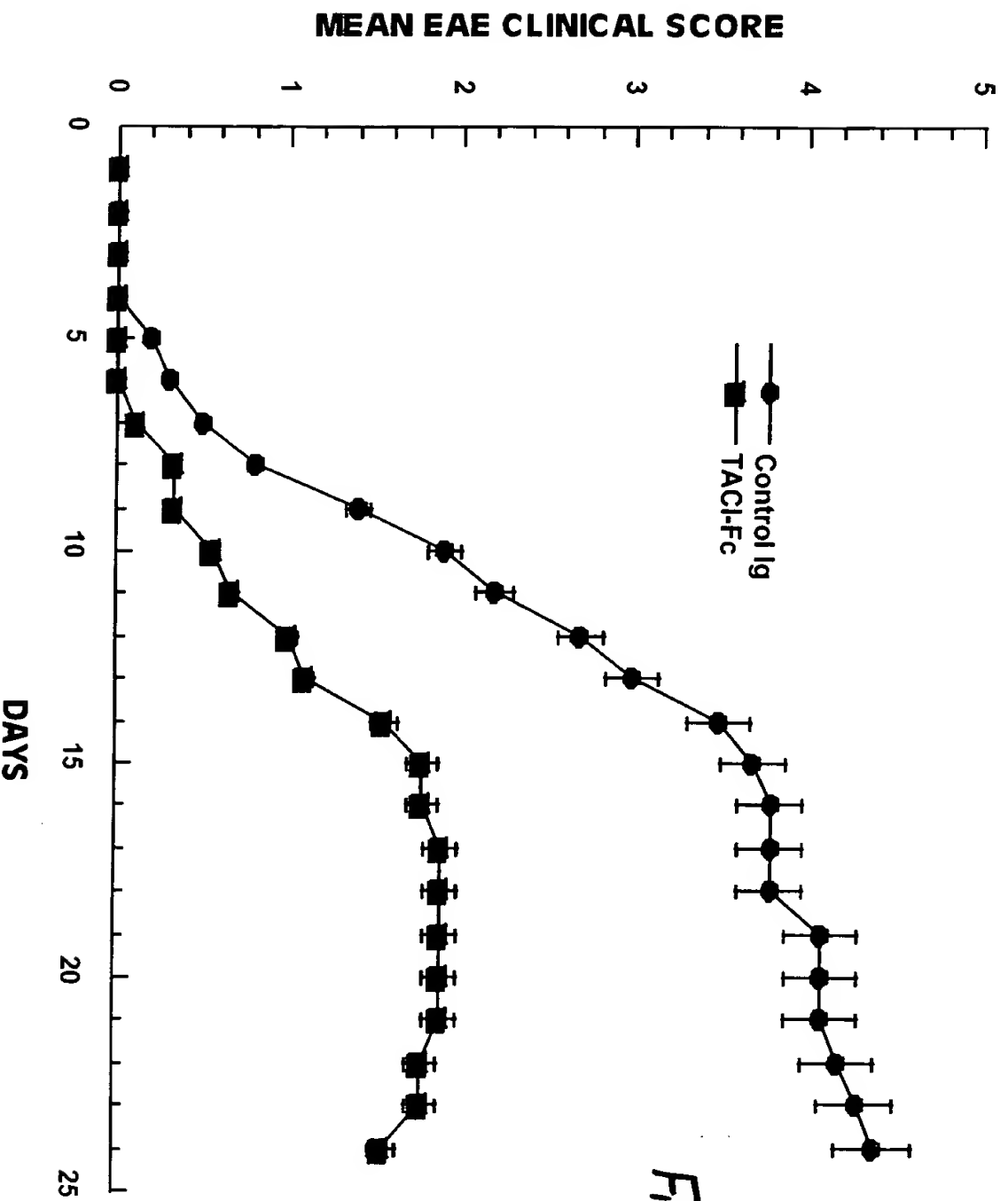


Fig. 20